

Applicants: Rothberg, *et al.*

U.S.S.N. 09/814,338

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Attorney Docket No. 21465-501 CIP2

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AMENDMENT

In the Specification:

Please amend the specification, without prejudice, as shown:

Please delete the paragraph on page 7, line 20-21 and replace it with the following paragraph:

FIGS. 1A-D are schematic illustrations of rolling circle based amplification using an anchor primer. **Figure 1B discloses a biotin-linker and template molecule as SEQ ID NOS 2 and 1 respectively. Figure 1C discloses a biotin-linker, SNP probe and a gene containing SNP as SEQ ID NOS 3, 4 and 5 respectively. Figure 1D discloses a biotin-linker and a template molecule as SEQ ID NOS 6 and 7 respectively.**

Please delete the paragraph on page 7, line 25-26 and replace it with the following paragraph:

FIG. 5 is a tracing of a sequence output of a concatemeric template generated using rolling circle amplification **(SEQ ID NO: 10).**

Please delete the paragraph on page 20, line 17 to page 21, line 2 and replace it with the following paragraph:

The use of a circular template and an anchor primer for identification of single nucleotide polymorphisms is shown in FIG. 1C. Shown is a generic anchor primer having the sequence 5' - gAC CTC ACA CgA Tgg CTg CAg CTT - 3' (SEQ ID NO:3). The anchor primer anneals to an SNP probe having the sequence 3'5' - TTT ATA TgT ATT CTA CgA CTC Tgg AgT gTg CTA CCg ACg TCg AAt CCg TTg ACT CTT ATC TTC A - 3' 5' (SEQ ID NO:4). The SNP probe in turn hybridizes to a region of a SNP-containing region of a gene having the sequence 3'5' - CTA gCT CgT ACA TAT AAA TgA AgA TAA gAT CCT g - 3' 5' (SEQ ID NO:5). Hybridization of a nucleic acid sequence containing the polymorphism to the SNP probe complex allows for subsequent ligation and circularization of the SNP probe. The SNP probe is

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designed so that its 5' and 3' termini anneal to the genomic region so as to abut in the region of the polymorphic site, as is indicated in FIG. 1C. The circularized SNP probe can be subsequently extended and sequenced using the methods described herein. A nucleic acid lacking the polymorphism does not hybridize so as to result in juxtaposition of the 5' and 3' termini of the SNP probe. In this case, the SNP probe cannot be ligated to form a circular substrate needed for subsequent extension.

Please delete the paragraph on page 54, line 29 to page 55, line 2 and replace it with the following paragraph:

The tandem repeat product in the extended sequence was identified by annealing a sequencing primer having the sequence 5'-AAGCTgCAGCCATCgTgTgAgg-3' (~~SEQ ID NO:8~~)(**SEQ ID NO:9**) and subjecting the annealed primer to 40 alternating cycles of 95 °C, 1 minute, 20 seconds, 60 °C using ET terminator chemistry (Amersham-Pharmacia) in the presence of 1M betaine.

Sequence Listing:

Please insert the Sequence Listing which is attached to this Amendment into the specification after page 54, but before the claims on page 55.

Amendments to the Drawings:

Please replace the drawings currently on file with "Replacement Sheets" for Figures 1A-5, submitted herewith.